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RESEARCH

The Influence Of Perianestesia Severe Critical Event On The Mortality Of Pediatric Patients Undergoing Anesthesia At Dr. Sardjito Hospital

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ABSTRACT

Background: severe critical events or unwanted and preventable incidents associated with anesthesia in pediatrics have a higher incidence rate compared with adults. It could be due to the immature anatomy, physiology, pharmacology, emotional, and social aspects of pediatric patients. In addition to the higher incidence, the mortality rate of severe critical events in pediatric patients is also higher than in adults. In general, severe critical events in pediatric patients include difficult airway, cardiovascular events, and medical negligence. Based on the time of occurrence, those events can happen pre-anesthesia, during anesthesia, or post-anesthesia with different incidence numbers.

Purpose: To assess the impact of critical events during peri-anesthesia on the mortality rate of pediatric patients. Such events include bronchospasm, laryngospasm, pulmonary aspiration, stridor, croup, desaturation, hypotension, arrhythmia, hemorrhage, cardiac arrest, anaphylaxis, neuro injury, delayed emergence, and medication errors.

Method: This is a prospective cohort study. All pediatric patients who underwent anesthesia for surgical and non-surgical procedures at RSUP Dr. Sardjito hospital are consecutively included in this study. The inclusion criteria for this study are pediatric patients less than 18 years of age who underwent anesthesia procedures at RSUP Dr. Sardjito hospital. The exclusion criteria are patients who have no complete medical records. The severe critical events included in this study are bronchospasm, laryngospasm, pulmonary aspiration, stridor, croup, desaturation, hypotension, arrhythmia, hemorrhage, cardiac arrest, anaphylaxis, neuro injury, delayed emergence, and medication errors. To statistically assess the relationship between severe critical events and mortality outcomes, bivariate analysis using chi-square was used. Multivariate analysis was then conducted using logistic regression on the variables that had a p-value of less than 0.25 on the bivariate analysis. A p-value of less than 0.05 indicates statistical significance.

Result: From the 425 research participants, 70 severe critical events happened in 39 patients, in which 14 cases resulted in mortality were recorded. The multivariate analysis showed that severe critical events of cardiac arrest (p=0,004; OR= 52,259; 95%CI= 3,505 – 779,081) and laryngospasm (p=<0,001; OR= 46,394; 95%CI= 6,001 – 358,640) significantly associated with patient mortality. Patient's demographic of ASA status (p=0,016; OR= 6,056; 95%CI= 1,403-26,139) and prematurity history (p=0,011; OR= 7,730; 95%CI= 1,607-37,193) are shown to be significantly associated with patient mortality.

Conclusion: There is a statistically significant relationship between severe critical events of cardiac arrest and laryngospasm with the mortality of pediatric patients who undergo anesthesia in RSUP Dr. Sardjito hospital.

Keywords: severe critical event, mortality, anesthesia, pediatric

Background

Anesthesia is an integral part of medical or surgical procedures. However, like other medical procedures, anesthesia can also cause complications and risks for patients, especially in pediatric patients. As a result of these risks, it is important for medical practitioners to understand the factors that may influence patient outcomes after anesthesia, including critical events that may occur during the peranesthesia period. RSUP Dr. Sardjito is one of the leading hospitals in Yogyakarta, Indonesia, which provides various types of medical procedures, including anesthesia for pediatric patients. One of the risks of anesthesia in pediatrics is the incidence of critical events that can cause morbidity and even mortality.

Severe critical event or critical incident is defined as an undesirable and preventable incident, which is related to the administration of general or regional anesthesia, and leads to, or can and/or has caused an undesirable outcome for the patient[(1)]. Severe critical events can happen to anyone, both adults and children. Children under one year of age have a higher incidence rate of experiencing a severe critical event than adults (4.6% compared to 1.2%)[(2)]. Based on the anesthesia practice in children observational trial (APRICOT) study of 31,127 pediatric patients in 261 European hospitals, reporting a high incidence (5.2%) of severe critical events in the perioperative period and wide variability[(3)]. The incidence of severe critical events and death is higher in patients undergoing emergency surgical procedures than in patients undergoing elective procedures. Several factors that can cause a severe critical event include the patient's preoperative status, incomplete equipment, emergency medications, and poor perioperative conditions[(4)].

Severe critical event in pediatric patients is different from adults. Infants generally experience severe critical events related to the respiratory system (laryngospasm, hypoxemia) and the cardiovascular system (arrhythmia)[(5)]. The incidence of severe critical events in pediatric anesthesia varies. The main risk factors that can be identified as being affected by a severe critical event are young age, previous medical history, and the patient's condition at the time of anesthesia and the procedure[(3)].

Based on research conducted by Lee et al., (2016) from a study conducted over 6 years, there were 229 severe critical events in 49,373 pediatric patients, with the respiratory system being the number one cause (55% of cases) due to tracheal-tube related events (40, 9%) and laryngospasm (17.3%). Apart from that, cardiovascular problems are also the main cause of severe critical events, such as cardiac arrest (66.7% of cases), cardiogenic shock

(16.7% of cases), and hypovolemic shock due to bleeding (16.7% of cases). Severe critical events related to human factors accounted for 58.5% of all critical incidents, with 53.7% of these factors related to the respiratory system[6].

Regarding the level of morbidity and mortality after the incidence of a severe critical event during anesthesia, there are several studies that support why this study needs to be carried out in Indonesia, including research conducted by Walter et al, which showed that at 30 days after surgery, 17.2% patients were reported to experience complications after treatment or surgery. Causes of death at 30-day follow-up included sepsis, multiorgan failure, congenital or acquired brain abnormalities, and respiratory failure[7]. Other research that supports this is research by Tariq et al., 2018 which states that severe critical incidents that specifically occur in the patient's respiratory system are the main cause of morbidity and mortality in pediatric patients undergoing anesthesia[8]. Furthermore, another study in Brazil found that the perioperative mortality rate for pediatric patients had increased over the last decade and the rate was higher in Brazil (9.8 per 10,000 anesthesia) and other developing countries (10.7-15.9 per 10,000 anesthesia). compared with developed countries (0.41-6.8 per 10,000 anesthesia) with the main risk factors including newborns or less than 1 year old, ASA III or more severe physical status, and undergoing emergency procedures, general anesthesia, or cardiac surgery. The main causes of child death in the study included problems with airway management and perioperative cardiovascular events[9].

Previous research mostly refers to severe critical events that occur in the respiratory and cardiovascular systems. However, this does not rule out the possibility that severe critical events that occur in other systems also contribute to increased mortality rates in pediatric patients undergoing anesthesia. In Indonesia, not many severe critical events have been reported which are often associated with patient mortality outcomes. This encourages researchers to raise this topic so that it can become an additional reference regarding pediatric anesthesia in the future.

Method

This research is a prospective cohort study of pediatric patients undergoing anesthesia at RSUP Dr. Sardjito. This research is nested from the study Factors that Influence the Occurrence of Major Complications After Anesthesia / Procedural Sedation in Pediatric Patients (Multicenter Study: Peri-Anesthetic Morbidity in Children in Asia (PEACH study) with ethical number KE/1356/10/2022. The information that will be collected is perioperative events, medical history data, anesthetic procedures, surgical procedures, and mortality data taken from direct examination and observation, medical record data or interviews with patient families at Dr. Sardjito Hospital who performed surgical and non-surgical procedures and required anesthesia after obtaining ethical clearance from the UGM FK-KMK Research Ethics Commission until the sample size was calculated using the proportion estimation formula from Riley et al., (2020) that the required sample size is 425 samples [10]. The data was checked, then coded, tabulated and inputed into the SPSS version 27 software program for data processing. In descriptive analysis, data on a categorical scale is expressed in frequency distribution and percentages. Data on a non-normally distributed numerical scale are displayed as median and maximum and minimum values. Analysis using chi-square and Mann Whitney test was carried out to determine the effect of severe critical events and subject characteristics on mortality. If p < 0.25, multivariable analysis will be carried out using multiple logistic regression and it is considered significant if p ≤ 0,05.

Result

Bivariate analysis was carried out to see the effect of severe critical events per anesthesia on mortality, the results of the analysis are presented in Table 1. Based on this table, it was found that severe critical events in the form of laryngospasm, bronchospasm, cardiac arrest, hypotension and desaturation had a significant effect (p≤0,05) on mortality events. Meanwhile, arrhythmia, bleeding, pulmonary aspiration, delayed emergence, and stridor have an insignificant effect on mortality.

The types of severe critical events with the highest case mortality rates were cardiac arrest (66.7%), stridor (33.3%), and laryngospame (28.6%). Meanwhile, the other severe critical event mortality rates are desaturation (22.2%), bronchospasm (18.2%), arrhythmia (16.7%) and hypotension (15.4%) as can be seen in Table 1. Besides thatSeveral other severe critical events have a mortality rate of 0%, including bleeding, pulmonary aspiration, and delayed emergence. In this study, no severe critical events were found in the form of anaphylaxis, nerve damage, croup and medication errors.

The results of the multivariate analysis with the double logistic regression test on the severe critical event variable which had a p value <0.25 in the bivariate analysis are shown in Table 2. The results of the analysis showed that the laryngospasm variable was (p=0.009) with an odds ratio (OR) value of 14.018 (CI 95% 1.920 – 102.323), cardiac arrest (p=0.009) with OR 43.165 (CI 95% 2.542 – 732.977) and desaturation (p=0.027) with OR 6.634 (CI 95% 1.228 – 35.550) independently and significantly influence the incidence patient mortality.

Bivariate analysis based on the characteristics of research subjects on the incidence of mortality, are shown in Table. Patients with ASA status >2 significantly influence the incidence of mortality with a risk 6.8 times greater than those with ASA status ≤2 (p =0.002; RR=6.8;95%CI=2.1-21.5). In addition, the presence of a history of congenital abnormalities in patients also significantly influences the incidence of mortality with a risk 3.4 times greater than patients without a history of congenital abnormalities (p=0.05; RR=3.4;95%CI=1.0-11.5).

The results of the bivariate analysis on both the severe critical event variable and subject characteristics on mortality were then undergo multivariate analysis. Variables that are analyse multivariately are variables that have a p value <0.25 in each bivariate analysis. These variables are laryngospasm, bronchospasm, cardiac arrest, hypotension, arrhythmia, desaturation, stridor, ASA status, history of prematurity, history of congenital abnormalities and premedication. These eleven variables were then analyzed multivariately with a multiple logistic regression test and the analysis results were obtained as presented in Table 4.

The results of multivariate analysis using a multiple logistic regression test showed that the variable laryngospasm (p=<0.001) had an odds ratio (OR) of 46.394 (CI 95% 6.001 – 358.640), cardiac arrest (p=0.004) with an OR of 52.259 (CI 95% 3.505 – 779.081) and history of prematurity (p=0.011) with OR 7.730 (CI 95% 1.607-37.193) and ASA status >2 (P=0.016) with OR 6.056 (CI 95% 1.403-26.139) independently and significantly influence the incidence of mortality patient.

In this study, there were a total of 70 severe critical events occurring in 39 patients, with an incidence rate of 9.17%. A total of 19 (4.5%) patients experienced one severe critical event, 11 (2.6%) patients experienced two severe critical events, 7 (1.6%) patients experienced three severe critical events, and 2 (0 .5%) patients experienced four severe critical events.

If we look at the distribution of time of occurrence in Table 5, the most severe critical events occurred during the duration of anesthesia, namely 37 incidents (52.8%). Where the types of severe critical events that most often occur during anesthesia are hypotension (29.7%) and desaturation (29.7%).

Post-anesthesia was the second most common time of occurrence which accounted for 20 (28.6%) severe critical events. Where the types of events that occur most frequently during post-anesthesia are laryngospasm (25%) and bronchospasm (20%).

Meanwhile, there were 13 (18.6%) severe critical events during pre-anesthesia, with desaturation (30.8%) and hypotension (23.1%) as the most common types of severe critical events during pre-anesthesia.

For the record, there was 1 patient who experienced one type of severe critical event in the form of hypotension at two different times, namely during pre- and during anesthesia. Apart from that, patients who experienced severe critical events in the form of hypotension and desaturation during the pre-anesthesia event were each given intervention in the form of fluid resuscitation and oxygenation using a face mask, so that the patients experienced an improvement in their condition and were still included in this study.

Discussion

Effect of Severe Critical Event Perianesthesia on Mortality

Of the total of 70 severe critical events that occurred in 39 patients, 14 cases ended in death. Based on these data it was found thatThe mortality rate for cases of severe critical events peri-anesthesia in pediatric patients at Dr Sardjito Hospital in this study reached 20%. When compared with several other studies, this mortality rate is still lower than the mortality rate for severe critical event cases in research in the Tribal Belt, India, which reached 28.57%[4]. However, it is still greater than the mortality rate for severe critical event cases in the NECTARINE study in Europe which only reached 3.2%[7]. The high mortality rate due to severe critical events in low and middle income countries compared to developed countries is likely due to a lack of standard perioperative monitoring, emergency medicines, equipment, preoperative preparation, and adequate training of health workers[11].

The type of severe critical event with the highest mortality rate in this study was cardiac arrest (66.7%),where 2 out of 3 (66.7%) patients who experienced cardiac arrest ended in death. In multivariate analysis of several *severe critical event* in this study showed that cardiac arrest had a statistically significant effect on the incidence of mortality compared to those who did not experience cardiac arrest with an increased risk of 52.2 times (p=0.004; OR=52.259; 95% CI=3.505 – 779.081). A similar thing was found in the study by Gupta et al (2009), where 4 out of 8 (50%) cases of cardiac arrest had an outcome in the form of mortality. The risk of perioperative cardiac arrest (POCA) increases greatly after anesthesia and surgery[12]. The main causes of POCA are classified based on the pathophysiology of origin, namely respiratory causes or hemodynamic changes during perioperatives[13]. Respiratory causes due to anesthesia related to cardiac arrest in pediatrics are still the most important cause compared to hemodynamic changes, this is due to the relatively narrow airways and the high incidence of respiratory tract infections in pediatrics(14). However, several conditions, including ASA physical status, cardiac surgery, emergency surgery, and duration of surgery, increase the risk factors for POCA (15). A meta-analysis showed that children aged less than one year, ASA physical status >3, and general anesthesia were independent predictors of perioperative cardiac arrest (11).

Stridor is a type of severe critical event related to respiration with the highest mortality rate, namely 33.3%, but has no statistical significance with mortality outcomes in either bivariate or multivariate analysis.Laryngeal edema, which has the potential to cause difficulty breathing and/or stridor after extubation, is one of themthe occurrence of PRAE which can ultimately cause desaturation and lead to death(16).

The mortality rate for severe critical events related to respiration in this study ranks next highest, namely laryngospasmwhere 2 out of 7 (28.6%) patients with laryngospasm died. The mortality rate for laryngospasm is higher than that found in researchGupta et al., (2009)namely 9.09% or 1 in 11 patients. Results of multivariate analysis of several *severe critical event* in this study showed that laryngospasm was significantly related to the incidence of mortality with a 14 times increased risk compared to those who did not experience laryngospasm (p=0.009; OR=14.018; CI 95%=1.920 – 102.323). Based on research conducted by Chekol and Melesse, (2020) it was stated that a history of airway anomalies, URTI infection, and inadequate depth of anesthesia were significantly associated with the incidence of laryngospasm. The use of inhaled anesthesia induction agents such as desflurane and isoflurane is also said to increase the incidence of laryngospasm in the pediatric age group. In addition, repeated attempts during airway placement increased the risk of laryngospasm 2.47 times greater than without repeated attempts.(17). Persistent perioperative laryngospasm can cause serious morbidity and mortality due to immediate events of hypoxia and hypoxemia such as heart attacks, or perioperative arrhythmias, or can cause delayed consequences in the form of negative pressure pulmonary edema resulting from upper or lower airway spasm or aspiration that occurs(18).

Desaturation is a type of severe critical event related to respiration with the next highest mortality rate and has a statistically significant influence on mortality outcomes. Based on bivariate analysis, it was found that patients who experienced desaturation had a 12.9 times increased risk of mortality compared to those who did not experience desaturation.(p=<0.001; RR=12.9; 95%CI=4.2-40.2).In this study, the mortality rate due to desaturation reached 22.2%, where 4 out of 18 patients (22.2%) with desaturation died. The mortality rate is slightly higher than in the studyGupta et al., (2009), which found that 2 out of 12 (16.67%) hypoxic patients died. In research conducted byWudineh et al., (2022)It was found that desaturation occurred in 50 (23.8%) patients and was the most common perioperative respiratory adverse event (PRAE). Where other PRAE events include laryngospasm, bronchospasm, apnea, coughing, and secretions can ultimately all cause desaturation. Persistent hypoxemia can result in potentially dangerous complications and even death. Desaturation occurs more often in babies because they have a higher oxygen demand and lower oxygen reserves so they are at risk of hypoxia. Apart from that, apnea or breath holding also often occurs in this group of patients because the respiratory center is not yet mature(16). Babies have irregular and periodic breathing patterns, breath holding often occurs in premature and term neonates and is different from clinical apnea. Some anesthetic medications, stimulation of laryngeal afferents during laryngoscopy or excessive lung inflation (Herring Breure inflation reflex) also contribute to prolonged apnea in neonates[19].

Bronchospasm contributed to the next highest mortality rate in severe critical event cases, namely with a mortality rate of 18.2% (2 out of 11 patients) and had a statistically significant effect. Based on bivariate analysis, it was found that patients who experienced bronchospasm had an 8.4 times increased risk of mortality compared to those who did not experience bronchospasm.(p=0.030; RR=8.4; 95%CI=2.0-34.3).The mortality rate for patients who experienced bronchospasm in this study was higher than the mortality rate for bronchospasm in the studyGupta et al., (2009)because in this study, the mortality rate for bronchospasm experienced by 6 patients was 0%. One possibility that could cause the difference in mortality rates is the patient's different medical history, starting from the patient's asthma status and its severity, history of upper respiratory tract infections in the last two weeks[20], type of surgery where thoracic and upper abdominal surgery has a higher risk, anesthesia modality where general anesthesia with tracheal intubation has a higher risk as well as history of GERD, and smoking status. During the peri-operative period, bronchospasm is common during induction of anesthesia. According toDewachter et al., (2011), bronchospasm can occur as a form of hypersensitivity reaction such as an anaphylactic reaction mediated by immunoglobulin E (IgE). However, it can also occur through non-allergic mechanisms, which may be triggered by pharmacological factors (via drugs that release histamine, such as atracurium or mivacurium and/or mechanical (bronchospasm induced by intubation). Whatever the causal mechanism, bronchospasm must be treated quickly. Because , if left untreated, bronchospasm can cause hypoxia, hypotension, and increased morbidity and mortality. When pure peri-operative bronchospasm occurs alone without other cardiovascular disorders, the oxygen concentration should be increased to 100% and manual bagging ventilation should be performed immediately to evaluate pulmonary compliance and identify. cause of high circuit pressure[22]. Increasing the concentration of inhalational anesthetics (sevoflurane, isoflurane) is often beneficial. Deepening of intravenous anesthesia (propofol) may be necessary, considering that intubation-induced bronchospasm may be due to lack of depth of anesthesia[23].

Hypotension is a severe critical event with the next highest death rate with 2 out of 13 (15.4%) hypotensive patients dying. Statistical significance was obtained from bivariate analysis with a p value of 0.041, in this study patients who experienced hypotension had a 7 times increased risk of mortality compared to those who did not experience hypotension (RR=7.0; 95%CI=1.7-29, 4). The death rate in this study was much smaller when compared to the death rate for hypotension cases in the studyGupta et al., (2009b)which reached 40.9% or 9 of 22 patients. This difference in mortality rates may occur due to differences in the patient's degree of illness before anesthesia, where children who are in critical condition or present with trauma, may not be able to tolerate intraoperative hypotension as well as children who are in healthy condition. Differences in the strictness of monitoring patients' vital signs can also contribute to differences in mortality rates. Prehospital hypotension is associated with increased mortality. The majority of recommendations define hypotension as systolic blood pressure below the 5th percentile for age. Mean blood pressure or mean arterial pressure (MAP) is an important determinant of tissue perfusion pressure. Therefore, MAP must be monitored, especially in children in critical condition, to serve as a guide for resuscitation or determining that blood pressure is too low. The MAP pressure value will vary depending on the child's height, so it needs to be adjusted for children who are too tall or short. However, in practice, systolic blood pressure is monitored more often than MAP(24), where most anesthetists define intraoperative hypotension as a 20-30% decrease in systolic blood pressure below the baseline threshold. Several other risk factors for pre-incisional hypotension are baseline hypotension, age (older children), induction with propofol, ASA ≥3, long pre-incision time(25).

The severe critical event with the next highest mortality rate was arrhythmia, namely 16.7% (1 in 6 patients). However, in bivariate analysis it was found that statistically the incidence of arrhythmias had no effect on the incidence of mortality, with a p value of 0.146 (RR=6.9; 95%CI=1.1-46.3). As a comparison, research by Gupta et al (2009) shows that the incidence of arrhythmias consisting of bradycardia, PSVT (Paroxysmal Supraventricular Tachycardia), and VT (ventricular tachycardia), has a mortality rate of 25% (1 in 4 patients). Arrhythmias sometimes occur in anesthesia of pediatric patients. In the past, when halothane was the primary inhalation agent, approximately 5% of pediatric patients experienced intraoperative arrhythmias. This happens because halothane makes the heart more sensitive to catecholamines, especially in conditions of hypercapnia, so that it becomes more pro-arrhythmic, especially arrhythmias originating from the ventricles. While sevoflurane is more commonly used as an inhalation induction agent and desflurane as a general anesthesia maintenance agent, there have been several cases of supraventricular tachycardia in previously healthy pediatric patients. However, even if intraoperative SVT occurs, it does not have a clinically significant relationship to patient morbidity(26). Another type of arrhythmia that often occurs is bradycardia, especially in infant patients compared to older pediatric patients. In fact, heart rate is the main determining factor in cardiac output in children under one year of age. If cardiac output decreases, fatal arrhythmias, cardiac arrest and even death can occur. Risk factors for post-induction bradycardia are hypoxia, premedication with opioids, inhalation induction (halothane), difficult intubation, intraoperative complications, and blood loss(27).

In this study, it was found that severe critical events such as bleeding, pulmonary aspiration, and delayed emergence had a mortality rate of 0% with a p value of 1.00 (RR=1.0; 95%CI=1.0-1.0). For the incidence of pulmonary aspiration, this is slightly different from the results of the studyGupta et al (2009)which shows that the mortality rate for pulmonary aspiration cases reaches 40% (2 out of 5 patients)(4).

If we look at the influence of research subject characteristics data on the incidence of mortality, it is found that ASA status >2 and a history of prematurity in multivariate analysis significantly influence the incidence of mortality. ASA status >2 increases the risk by 6 times for experiencing mortality compared with ASA status ≤2 (p=0.016; OR= 6.056; 95%CI= 1.403-26.139) as well as a history of prematurity increasing the risk by 7.7 times for experienced mortality compared with those without a history of prematurity (p=0.011; OR=

7.730; 95%CI= 1.607-37.193). Other studies also show that a higher ASA classification increases the likelihood of a heart attack where the incidence of cardiac arrest in patients with ASA status 3-4 is 0.194% (19.44/10,000) compared to patients with ASA status 1-2 0.018% (1.81 /10,000). Patients with ASA status III-V are the sole cause of death in most studies because they consistently have an increased risk of heart attack compared to other ASA statuses [(28)]. In another study, it was found that a history of prematurity contributed to 28.6% of the incidence of PRAE, this is because premature babies have an immature respiratory center[(16)]. Breath holding or apnoeic spell is defined as a pause in breathing of up to 20 seconds associated with bradycardia and/or cyanosis. This event is related to gestational age and occurs more often in premature neonates. Anesthetic agents are one of the factors that can worsen apnea spells in premature babies[(29)]. The combination of immature respiratory system development, disease and anesthesia increases the likelihood of hypoxia in premature babies. In addition, premature babies have a small absolute blood volume and therefore relatively small blood loss during surgery can quickly lead to hypovolemia, hypotension and shock. Autoregulation is also not well developed in premature babies and the heart rate may not increase due to hypovolemia and also the presence of anesthetic agents can blunt the baroreflex in premature babies thereby further limiting the ability to compensate for hypovolemi[(29)]. Babies with less than a month's gestational age are more likely to have congenital abnormalities that previously required respiratory assistance, thus contributing to perioperative cardiovascular instability and even death[(7)].

The presence of a history of congenital abnormalities in patients also significantly influences the incidence of mortality. In the bivariate analysis of this study, it was found that the presence of a history of congenital abnormalities increased the risk by 3.4 times of experiencing mortality compared to patients without a history of congenital abnormalities (p=0.05; RR =3.4; 95%CI=1.0-11.5). In a study conducted by Walker et al., (2022) it was found that the incidence of perioperative cardiovascular instability was reported in 130 patients during 148 episodes of anesthesia, of which 130 patients included patients who were born prematurely, had congenital abnormalities that previously required respiratory assistance or congenital heart defects. patent ductus arteriosus[(7)]. Children with congenital abnormalities, especially congenital heart disease, have a higher risk of experiencing perioperative side effects than children who do not suffer from congenital heart disease. In research by Foz et al., (2023) it was found that patients with severe congenital heart disease had a much higher risk of experiencing a heart attack. This is in line with the Pediatric Perioperative Cardiac Arrest (POCA) recording, where 34% of patients who experience anesthesia-related heart attacks suffer from congenital heart disease [(28)].

Time Distribution of Severe Critical Events

The incidence rate of severe critical events peri-anesthesia in pediatric patients at Dr Sardjito Hospital in this study reached9.17%. This figure is lower than the incidence of severe critical events in pediatric patients in Togo, Sub-Saharan Africa, which reached 49%[(30)]. This may happen because in that study 75.2% of the actions were emergency actions, whereas in this study there were only 3.8% emergency actions. In addition, 75.2% of anesthesia was carried out only by anesthesia nurses, which is different from this study where 97.4% of procedures were carried out by anesthesia resident doctors under supervision.This figure is also still lower than the incidence rate from the audit of anesthesia practices in neonates and children (NECTARINE) in Europe which reached 35.3%[31]. This might happen because the research subjects were neonates and babies, with the average age of the research subjects being 48 days, which is different from this study where the majority (43.8%) of the research subjects were aged 5-18 years. In addition, 43.8% of pediatric patients had congenital abnormalities, in contrast to this study which was only 33.9%.However, this figure is still higher than the incidence rate from the APRICOT study which was also carried out in Europe, which was only 5.2%[32], as well as at the Wilhelmina Children's Hospital in the Netherlands which was only 3.4%[5].

Based on the time of occurrence, severe critical events can be grouped into pre-anesthesia, durante anesthesia, and post-anesthesia. In this study, it was found that the most severe critical events occurred during the duration of anesthesia, namely 37 incidents (52.8%). Similar things were found in researchSarakawabalo et al., (2023), where severe critical events occurred more frequently intraoperatively (78.1%) than postoperatively (21.9%). When classified further, according to researchEngelhardt et al., 2019, severe critical events occurred more frequently during the maintenance period of anesthesia (67.3%-69.8%) than during the induction period (20.9%-27.6%), wake-up period (2%-5.3%), or recovery period (3.1%-4.0)[3].

In this study, the most frequent severe critical events during pre-anesthesia and during anesthesia were desaturation and hypotension. The incidence of pre-anesthesia hypotension in this study occurred in three patients who had ASA III status and if we look at the operation and type of anesthesia used, two of them underwent major surgery with general anesthesia. Meanwhile, in the case of hypotension during anesthesia, it was found that 6 out of 11 people who experienced hypotension during anesthesia had ASA III status and if we looked at the operation and type of anesthesia used, 9 out of 11 patients underwent major surgery with general anesthesia. Intraoperative hypotension occurs more often in patients receiving general anesthesia, especially in the post-induction and pre-incision periods, this is because some anesthetic induction agents can trigger hypotension[24]. Some of the main factors that contribute to hypotension during anesthesia are excessive depth of anesthesia, blood loss (due to excessive bleeding during surgery), vasodilation (due to anesthetic agents), decreased cardiac output (due to bradycardia or decreased stroke volume), increased intra-thoracic pressure (due to mechanical ventilation), failure of the sympathetic nervous system or baroreflex system[33][34]. Several other factors were also found to be associated with intraoperative hypotension in children, namely fasting status, ASA status, preoperative hypotension, intravenous induction, propofol dose and body mass index (BMI)[35]. In research conducted by Nafiu et al., 2010, it was stated that the prolonged interval between the induction of anesthesia and the start of the surgical incision was one of the factors that contributed to the incidence of intraoperative hypotension, especially in children with a high body mass index (BMI). In other studies the same thing was found where baseline hypotension, age (older children), induction with propofol, ASA status≥3, long pre-incision time is another risk factor for pre-incisional hypotension [25].

The incidence of pre-anesthesia desaturation in this study occurred in four patients who had ASA status II and III, if seen based on the operation and type of anesthesia used, three of them underwent major surgery with general and combination anesthesia. Meanwhile, in the case of anesthesia duration desaturation, it was found that 6 out of 11 people who experienced anesthesia duration desaturation had ASA III status and if we looked at the surgical procedure and type of anesthesia used, 6 out of 11 patients underwent major surgery with general and combination anesthesia.On researchDisma et al., (2021)It was found that hypoxaemia episodes occurred more frequently during the maintenance of anesthesia period (55%) compared to the induction period (26%) or wake-up period (15%).The causes of desaturation that occur during induction can be quickly identified, such as laryngospasm, difficult intubation, and inadequate ventilation. Desaturation often occurs after tracheal intubation, this is because some anesthetic agents are known to reduce respiratory drive, which can lead to hypoxemia.. In a study by Oofuvong et al., (2014) it was found that several causes of intraoperative desaturation were light anesthesia (children who were not anesthetized adequately) with the installation of an endotracheal tube (31%), laryngospasm (26%), bronchospasm (22%), Prolonged apnea during laryngoscopy (12%), accidental extubation (4%), endobronchial intubation (1.4%) and Upper Airway Obstruction (1.4%). In this study it was described that light anesthesia with an ETT placed during the maintenance period (31%) was the most common cause of desaturation, which may be triggered by position or surgical stimulation during the first 15 minutes. Being on your side doubles the risk of desaturation compared to lying on your back. Laterality can affect ventilation and perfusion compliance and easily lead to desaturation that is exacerbated by light anesthesia. The second most common cause of desaturation is laryngospasm (26%). High levels of laryngospasm are seen in the first 30 minutes when airway stimulation may trigger laryngospasm during surgical stimulation(36). Apart from that, other factors such as ASA status also increase the risk of intraoperative desaturation. In research conducted by (Charuluxananan, 2007) it was found that patients with ASA status classifications of 3, 4, and 5 had an increased risk of intraoperative desaturation(16).

The most common severe critical events occurring during post-anesthesia are laryngospasm and bronchospasm. This is similar to research conducted byWudineh et al., (2022)where laryngospasm and bronchospasm most commonly occur after extubation, this is associated with airway secretions and a history of previous ARI comorbidities. Morphological damage to the epithelium and mucosa of the airways after infection makes the airways more sensitive to potentially irritating anesthetic gases and secretions, causing activation of irritant receptors and contraction of airway smooth muscle(16). Several anesthetic factors such as anesthesia conditions that are not yet deep when the stimulus occurs, the use of more irritating anesthetic gases such as isoflurane or desflurane, the presence of blood or secretions in the airway, airway instrumentation when anesthesia is not yet deep, the use of LMA, and the insufficiency of the anesthesiologist, especially when dealing with pediatric patients can increase the risk of laryngospasm(37). Perioperative respiratory adverse events (PRAE), namely laryngospasm, bronchospasm and airway secretions, can ultimately cause desaturation and have the potential to be dangerous or even death (16). The same thing was also found in research conducted by Visvanathan et al., (2005) that, Laryngospasm is a significant problem in anesthesia where almost half of it is caused by airway manipulation such as inserting a laryngeal mask, oropharyngeal airway, extubation and suction. The incidence of laryngospasm occurs due to late recognition and intervention which then causes desaturation, postoperative pulmonary edema, failure to deepen anesthesia with intravenous agents, continued use of irritant volatile agents[(22)].

In this study, it was found that severe critical events that occurred during anesthesia contributed the most to patient mortality, where 71.43% (10 of 14) deaths were related to severe critical events that occurred during anesthesia. Meanwhile, 28.57% (4 of 14) deaths were related to severe critical events that occurred after anesthesia. This finding is different from other studies which show that the highest death rate occurs after anesthesia. Research by Tarekegn (2021) shows that the mortality rate within 24 hours, 48 hours and 7 days after surgery for pediatric patients is getting higher over time, namely 0.59%, 1.42% and 2.58%[(38)]. Similar results were found in research by Van Der Griend (2011) which showed that mortality within 24 hours and 30 days after administering anesthesia was 13.4 per 10,000 procedures and 34.5 per 10,000 procedures[(39)]. Likewise in research by Talabi (2021), where the mortality rate within 24 hours, 7 days and 30 days after surgery for pediatric patients was 113.2 per 10,000 procedures (95%CI=40-210), 207.6 per 10,000 procedures (95%CI=110-320), and 320.8 per 10,000 procedures (95%CI=190-470) respectively. This may occur due to the patient's pre-operative condition which is complicated by the presence of sepsis[(40)].

The limitation of this research is the lack of monitoring of severe critical events when the patient has been sent home to the treatment room because this research was carried out only from the time the patient was received in the operating room reception room until the patient was sent home from the recovery room so it could not describe the influence of a severe critical event in real terms. whole.

Conclusion

Based on this research, the occurrence of severe critical events, laryngospasm, cardiac arrest, and desaturation influence mortality of pediatric patients undergoing anesthesia at RSUP Dr. Sardjito.

Suggestion

Further research needs to be carried out with longer monitoring time so that a more adequate scoring and monitoring system for severe critical events and its effect on mortality can be developed.

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Table and Figure

Table 1. Bivariate Analysis Severe Critical Events and Mortality Rates

Severe Critical Event	Mortality Death n (%)	No n (%)	*P-value*	RR (95%CI)
Laryngospasm				
Yes	2 (28,6%)	5 (71,4%)	**0,012*ᵃ**	13,3 (3,5-50,6)
No	9 (2,2%)	409 (97,8%)		
Bronchospasm				
Yes	2 (18,2%)	9 (81,8%)	**0,030*ᵃ**	8,4 (2,0-34,3)
No	9 (2,2%)	405 (97,8%)		
Anaphylaxis				
Yes	0 (0,0%)	0 (0,0%)	-	-
No	11 (2,3%)	414 (97,4%)		
Nerve Damage				
Yes	0 (0,0%)	0 (0,0%)	-	-
No	11 (2,3%)	414 (97,4%)		
Cardiac Arrest				
Yes	2 (66,7%)	1 (33,3%)	**0,002*ᵃ**	31,3 (11,2-87,4)
No	9 (2,1%)	413 (97,9%)		
Hypotension				
Yes	2 (15,4%)	11 (84,6%)	**0,041*ᵃ**	7,0 (1,7-29,4)
No	9 (2,2%)	403 (97,8%)		
Arrhythmia				
Yes	1 (16,7%)	5 (83,3%)	0,146ᵃ	6,9 (1,1-46,3)
No	10 (2,4%)	409 (97,6%)		
Haemorrhage				
Yes	0 (0,0%)	3 (100,0%)	1,000	1,0 (1,0-1,0)
No	11 (2,6%)	411 (97,4%)		
Medication errors				
Yes	0 (0,0%)	0 (0,0%)	-	-
No	11 (2,3%)	414 (97,7%)		
Pulmonary Aspiration				
Yes	0 (0,0%)	2 (100,0%)	1,000	1,0 (1,0-1,0)
No	11 (2,3%)	412 (97,4%)		
Croup				
Yes	0 (0,0%)	0 (0,0%)	-	-
No	11 (2,6%)	414 (97,4%)		
Desaturation				
Yes	4 (22,2%)	14 (77,8%)	**<0,001*ᵃ**	12,9 (4,2-40,2)
No	7 (1,7%)	400 (98,3%)		
Delayed Emergence				
Yes	0 (0,0%)	3 (100,0%)	1,000	1,0 (1,0-1,0)
No	11 (2,6%)	411 (97,4%)		
Stridor				
Yes	1 (33,3%)	2 (66,7%)	0,076ᵃ	14,1 (2,5-78,05)
No	10 (2,4%)	412 (97,6%)		

Becausethere are cells that have an expected value <5, then the analysis is carried out using Fisher Exact
*The variable is statistically significant with p≤0.05
[a]Variables with p<0.25 in bivariate analysis will be tested multivariately.

Table 2. Multivariate Analysis Severe Critical Events and Mortality Rates

Variable	Coefficient	Standard Error	P-value	OR	95% CI
Laryngospasm	2,640	1,014	**0,009***	14,018	1,920 – 102,323
Cardiac Arrest	3,765	1,445	**0,009***	43,165	2,542 – 732,977
Desaturation	1,892	0,857	**0,027***	6,634	1,228 – 35,550

*The variable is statistically significant with p≤0.05

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Variable	Mortality Yes n (%)	Mortality No n (%)	Amount n (%)	p-*value*	RR (95%CI)
Age					
<1 years	4 (4,3)	88 (95,7)	92 (100)		
> 1 – 5 years (*childhood*)	4 (2,7)	142 (97,3)	146 (100)	0,353	-
>5 - <18 years	3 (1,6)	184 (98,4)	187 (100)		
Height	11 (2,6)	414 (97,4)	425 (100)	0,268	-
Mean Rank	172,55	214,07			
Weight	11 (2,6)	414 (97,4)	425 (100)	0,396	-
Mean Rank	181,95	213,82			
Sex					
Man	5 (2,0)	251 (98,0)	256 (100)	0,358	0,5 (0,2-1,8)
Women	6 (3,6)	163 (96,4)	169 (100)		
ASA state					
ASA >2	6 (9,4)	58 (90,6)	64 (100)	**0,002***[a]	6,8 (2,1-21,5)
ASA ≤2	5 (1,4)	356 (98,6)	361 (100)		
History of prematurity					
Yes	3 (7,3)	38 (92,7)	41 (100)	0,08[a]	3,5 (0,9-12,7)
No	8 (2,1)	376 (97,9)	384 (100)		
History of comorbidities					
Yes	2 (4,5)	42 (95,5)	44 (100)	0,318	1,9 (0,4-8,6)
No	9 (2,4)	372 (97,6)	381 (100)		
History of congenital abnormalities					
Yes	7 (4,9)	137 (95,1)	144 (100)	**0,05***[a]	3,4 (1,0-11,5)
No	4 (1,4)	277 (98,6)	281 (100)		
Premedication					
Ya	1 (10)	9 (90)	10 (100)	0,233[a]	4,1 (0,6-29,4)
Tidak	10 (2,4)	405 (97,6)	415 (100)		
Type of anesthesia					
Sedation	4 (2,1)	185 (97,9)	189 (100)		
General	6 (2,9)	199 (97,1)	205 (100)	0,642	-
Regional	0 (0,0)	3 (100)	3 (100)		
Combination	1 (3,6)	27 (96,4)	28 (100		
Anesthesia Operator					
Anesthesia specialist	0 (0,0)	11 (100)	11 (1000	1,000	1,0 (1,0-1,0)
Resident with supervision	11 (2,7)	403 (97,3)	414 (100)		
Anesthesia Services					
Operating room	7 (2,2)	305 (97,8)	312 (100)		
Outside the operating room	4 (3,5)	109 (96,5)	113 (100)	0,493	0,6 (0,2-2,1)
Urgency of Action					
Elective	10 (2,4)	399 (97,6)	409 (100)	0,348	0,4 (0,05-2,9)
Emergency	1 (6,3)	15 (93,8)	16 (100)		
Action Type					
Mayor	4 (3,5)	109 (96,5)	113 (100)	0,493	1,6 (0,5-5,3)
Non-mayor	7 (2,2)	305 (97,8)	312 (100)		

Table 3. Bivariate Analysis of Subject Characteristics and Mortality Rates

Because there are cells that have an expected value <5, then the analysis is carried out using Fisher Exact

TB and BW data were analyzed using the Mann Whitney test because numerical data was not normally distributed.

The analysis table for age and type of anesthesia is not in a 2x2 format so an RR value cannot be obtained.

*The variable is statistically significant with p≤0.05

[a]Variables with p<0.25 in bivariate analysis will be tested multivariately.

ASA: American Society of Anesthesiologists

Table 4. Analisis Multivariat Faktor-Faktor yang Berpengaruh dengan Mortalitas

Variable	Coefficient	Standard Error	P- value	OR	95% CI
Laryngospasm	3,837	1,043	**<0,001***	46,394	6,001 – 358,640
Cardiac arrest	3,956	1,379	**0,004***	52,259	3,505 – 779,081
History of prematurity	2,045	0,802	**0,011***	7,730	1,607-37,193
ASA status >2	1,801	0,746	**0,016***	6,056	1,403-26,139

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*The variable is statistically significant with p≤0.05
ASA: American Society of Anesthesiologists

Table 5 .Distribution of Severe Critical Events Based on Time of Event 56

Severe Critical Event	Time of Event			Total Events n (%)
	Pre-Anaesthesia n (%)	Durante Anesthesia n (%)	Post Anesthesia n (%)	
Laryngospasm	1 (0,2%)	1 (0,2%)	5 (1,2%)	7 (1,6%)
Bronchospasm	2 (0,5%)	5 (1,2%)	4 (0,9%)	11 (2,6%)
Anaphylaxis	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)
Nerve Damage	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)
Cardiac Arrest	1 (0,2%/)	2 (0,5%)	0 (0,0%)	3 (0,6%)
Hypotension	3 (0,7%)	11 (2,6%)	0 (0,0%)	14 (3,3%)
Arrhythmia	1 (0,2%)	4 (0,9%)	1 (0,2%)	6 (1,4%)
Bleeding	0 (0,0%)	3 (0,7%)	0 (0,0%)	3 (0,7%)
Medication errors	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)
Pulmonary Aspiration	1 (0,2%)	0 (0,0%)	1 (0,2%)	2 (0,5%)
Croup	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)
Desaturation	4 (0,9%)	11 (2,6%)	3 (0,7%)	18 (4,2%)
Delayed Emergence	0 (0,0%)	0 (0,0%)	3 (0,7%)	3 (0,7%)
Stridor	0 (0,0%)	0 (0,0%)	3 (0,7%)	3 (0,7%)

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